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CERTIFICATE OF MAILING

I hereby certify that on November 21, 2002, this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service in accordance with 37 C.F.R. § 1.10 as first class mail with sufficient postage in an envelope addressed to: Commissioner for Patents, Washington, DC 20231.

Trudi Thompson

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PATENT

Applicant: **Manning et al.**
Serial No.: **09/665493**
Filed: **September 20, 2000**
Title: **USE OF RECOMBINANT GENE DELIVERY VECTORS FOR TREATING OR PREVENTING DISEASES OF THE EYE**
Examiner: **T. Ton**
Group Art Unit: **1646**
Atty Docket No.: **20263.40**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

NOTICE TO COMPLY

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TECH CENTER 1600/2900

Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Notice to Comply dated October 16, 2002, Applicants respond as follows:

On page 34, beginning at line 5:

The pD10 AAV vector is constructed by replacing the AAV gene encoding sequences of pD-10 (see Wang, X. et al., J. Virol. 71:3077 (1997), with the CMV promoter, multiple cloning site, and BGH polyadenylation sequences from pKm201CMV. Briefly, oligonucleotides 5'-ggtatttaaa acttgcggcc gcggaatttc gactctaggc c-3' (SEQ I.D. No. 9) and 5'-gctgcccggg acttgctagc tggatgatcc tccagcgcgg ggatctcatg -3' (SEQ I.D. No. 10) are used to amplify the CMV expression cassette from pKm201CMV. The product of this PCR amplification is digested with SmaI and DraI and cloned into pD-10 digested with EcoRV. This new vector is named pD-10CMV.

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On page 37, beginning at line 25:

Oncogenic activity is associated with the wild-type FGF-5 molecule (Zhan et al., 1988; Bates et al., 1991). To improve its safety, the codons for the first 21 amino acids of FGF-5's signal sequence were removed by PCR amplification of the above pD10-CMV-FGF-5 plasmid with the following primers:

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AGA/TAT/AAG/CTT/ACC/ATG/GGT/GAA/AAG/CG T/CTC/GCC/CCC/AAA (5',

5FGFMUTB; SEQ I.D. No. 11) and CGC/GCG/CTC/GAG/AC C/ATG/AGG/AAT/ATT/AT C/CAA/AGC/GAA/ACT (3', 3FGF5WT; SEQ I.D. No 12). The 5' primer contains point mutations which destabilize G/C rich hairpin structures of the FGF-5 mRNA, and should increase levels of gene expression. The PCR product was digested with HindIII and XhoI (restriction sites introduced by the primers), and cloned by standard methods, into the pD10 vector digested with the same enzymes. The pD10-CMV-FGF-5 (sig-) vector is illustrated schematically in Figure 5.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changed made**."

It is believed that no fees are due with this filing. If fees are due, the Commissioner is hereby authorized to charge payment of any additional filing fees or credit any overpayment to Deposit Account No. 50-1901. A duplicate copy of this sheet is attached.

Respectfully submitted,

November 20, 2002

Louis C. Cullman
Registration No. 39,645

OPPENHEIMER WOLFF & DONNELLY LLP
840 Newport Center Drive, Suite 700
Newport Beach, California 92660
Telephone: 949.823-6000
Facsimile: 949.823-6100